Research Article

Infant Mortality among Twins from the Pelotas 2004 and 2015 Birth Cohorts

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Abstract

Objective: To describe the prevalence of multiple pregnancies and compare first- and second-born twins to each other and to singletons, in terms of infant mortality.

Methods: The 2004 and 2015 Pelotas Birth Cohorts are population-based studies conducted in Pelotas, South Brazil. A monitoring system was assembled to detect all deaths of cohort participants in the first year of life. Infant Mortality Rate (IMR):1000 live births (LB) and its components (neonatal and post-neonatal mortality rates) were calculated.

Results: Among 4,187 pregnancies in 2004 and 4,220 in 2015, respectively, 42 (1.0%) and 56 (1.3%)

were multiple. Eighty-four twins were born alive in 2004 and 111 in 2015. The majority of twin pregnancies failed to reach 37 weeks (61.9% in 2004 and 82.2% in 2015). Prevalence of twin births < 34 weeks of gestation more than doubled from 2004 (19.0%) to 2015 (42.1%) (p=0.03). In the 2004 cohort, there were 79 infant deaths, three of which were twins, and in the 2015 cohort, among the 57 deaths, five were of twins. In the 2004 cohort there was no difference in IMR between twins and singletons. In the 2015 cohort, IMR in first-born twins was similar to that of singletons, whereas among second-born twins, the IMR was six times higher than in singletons (75.4:1,000 LB *versus* 12.5:1000 LB).

Conclusion: While improvements in medical care may have led to improved survival among infants born at less than 34 weeks, these infants are still at increased risk of dying before reaching one year of age.

Keywords: Twins; Multiple Pregnancies; Cohort Studies; Prematurity; Infant Mortality

1. Introduction

Twin births represent 2-4% of pregnancies in the world [1]. In recent decades, due to the growing popularity of assisted reproduction techniques such as in vitro fertilization and intrauterine insemination, there has been an increase in the number of multiple pregnancies, especially in developed countries [2]. In Brazil, according to data from the Information System on Live births (SINASC), the national rate is 1.1%, with regional variations, reaching 2.5% in some of Brazil's larger cities [3]. Previous studies showed that twin pregnancies are associated with higher risks of preterm birth, low birthweight (LBW), intrauterine growth restriction, and umbilical cord prolapse [4, 5]. As a result, the intrapartum and perinatal mortality rates are three and seven times higher, respectively, among twins compared to singletons [6]. Birth order in twin pregnancies has also been investigated as a risk factor for newborns. Lower birthweight and higher perinatal mortality were observed in second-born compared to first-born twins [5, 7-10], mainly due to hypoxia and prolonged labor [11-14]. Therefore, based on data from the 2004 and 2015 Pelotas Birth Cohorts, the aim of this study was to describe the prevalence and duration of multiple pregnancies and compare first- and second-born twins to each other and to singletons, in terms of infant mortality rate (IMR).

2. Material and Methods

Two population-based cohort studies in Pelotas, Brazil, aimed to include all hospital births in the city in the years 2004 and 2015. The recruitment strategies and data collection methods were very similar in the two cohorts [15, 16]. Briefly, from January 1^{st} to December 31^{st} in 2004 and 2015, all five hospitals with maternity departments in the city were visited daily by the research team. All newborns of mothers living in the urban area were eligible to the cohorts. Children born outside the hospital (fewer than 2% in the two cohorts) were also included, since the mothers normally came to the maternity department soon after giving birth, when they were included in the study. The mothers were interviewed during their hospital stay (perinatal survey) in the first 24 hours postpartum by trained interviewers, who applied previously tested structured questionnaires. Enrollment totaled 4,231 children in 2004 and 4,275 in 2015. In the perinatal interview, data were collected on family income in minimum wages in the month prior to delivery (later coded as ≤ 1, 1.1-3.0, 3.1-6.0, 6.1-10, and > 10 minimum wages) and maternal characteristics: schooling in complete years (later coded as < 4, 4-8, 9-11, and ≥ 12 years), age (< 20, 20-24, 25-29, 30-34, and ≥ 35 years), self-reported skin color (white, brown, or black), parity (primipara, secondipara, or multipara), type of delivery (vaginal or cesarean), type of gestation (singleton or multiple), and complications in the pregnancy (arterial hypertension, diabetes mellitus, third-trimester bleeding, and premature rupture of membranes).

Newborns were weighed by the hospital team using pediatric scales, SECA model 376, which were calibrated regularly by the study team. LBW was defined as birthweight less than 2,500 grams and extremely low birthweight (ELBW) as birthweight less than 1,500 grams. Length was measured by the research team using an ARTHAG infantometer in 2004 and a Harpenden infantometer in 2015, both with precision to 1 mm. In the 2004 cohort, gestational age was calculated from the date of last menstruation (DLM), as long as consistent with the infant's weight, length, and head circumference at birth, in relation to the normal curves for these parameters for each week of gestational age [17]. If the gestational age based on DLM was unknown or inconsistent, maturity was estimated by ultrasound, as long as it had been performed prior to the 20th gestational week and recorded on the pregnant woman's prenatal card, and based on the Dubowitz method [18], which was applied to all the newborns.

In the 2015 cohort, gestational age was calculated on the basis of DLM and obstetric ultrasound tests (about 85% of the mothers had ultrasound records from the first or second trimester) [19]. For the analysis, gestational age was divided into three categories: < 34, 34-36, and ≥ 37 weeks. Five-minute Apgar score less than 7 and admission to neonatal intensive care unit (NICU) were extracted from the hospital files. Birth order of twins was obtained from the time of birth recorded on the newborn files. A monitoring system was assembled to detect all deaths of cohort participants in the years 2004 and 2005 (for the 2004 cohort participants) and in the years 2015 and 2016 (for the 2015 cohort participants). Regular visits were made to the city's hospitals, where intensive care units, maternity departments, pediatric wards, and emergency departments were visited. Deaths outside the hospital setting were tracked in the vital statistics records of the municipal health department.

In the analyses, the two cohorts were initially compared in terms of family income and maternal characteristics. Then, for each cohort, the prevalence of multiple pregnancies according to family income and maternal characteristics and the duration of singleton and multiple pregnancies were calculated. In these analyses, the denominator was the number of mothers in each cohort. Later, the first- and second-born twins from the same cohort were compared to each other and to the singleton newborns in terms of birthweight, 5-minute Apgar score, NICU admissions, neonatal mortality rate (NNMR) (0-27th day of life), post-neonatal mortality rate (PNMR) (28th to 364th day of life), and IMR (0-364th day of life) per 1,000 live births (LB). In these analyses, the denominator was the number of newborns in each cohort. Newborns from triplet pregnancies were excluded from these analyses. Means and standard deviations (SD) were calculated for the continuous variables, and proportions and 95% confidence intervals (95%CI) for the categorical variables. Student t-tests were used to compare the means, and chi-square tests to compare heterogeneity of categorical variables. The Weinberg method was used to estimate the number of monozygotic and dizygotic pairs [20]. According to this method, the dizygotic twin rate is double the rate of twins in which the pairs' sex is discordant, and the rate of monozygotic twin pregnancies is calculated as the difference between the total number of twin pregnancies and the dizygotic rate. The perinatal study of the 2004 cohort was approved by the Institutional Review Board of the School of Medicine, Federal University of Pelotas (protocol 40601116), and the perinatal study of the 2015 cohort was approved by the Institutional Review Board of the School of Physical Education, Federal University of Pelotas (protocol 26746414. 5.0000.5313). The mother or the child's legal guardian signed the free and informed consent form before the data were collected.

3. Results

Among the 4,187 pregnancies in the 2004 cohort, 42 (1.0%) were multiple; and among the 4,220 pregnancies in the 2015 cohort, 56 (1.3%) were multiple, two of which were triplet pregnancies. Of the multiple pregnancies, 84 twins were born alive in 2004 and 111 in 2015. In 2004, the estimated rate of dizygotic pairs was 34%, and in 2015 it was 62%. More than one third (67.9%) of the mothers in the 2004 cohort and more than half (59.9%) of those in the 2015 cohort belonged to families with monthly income ≤ 3 minimum wages (Table 1). The proportion of women from families that earned one minimum wage or less decreased by half during the period (from 24.1% in 2004 to 12.7% in 2015; $p < 0.001$). There was a major change in education from 2004 to 2015, whereby the proportion of mothers with more schooling (12 years or more) tripled during the period (from 10.1% to 31.0%). As for age, in 2015 there was an increase in the proportion of mothers 30-34 years of age (from 17.9% in 2004 to 23.4% in 2015). The proportion of mothers with self-reported white skin color increased from 2004 to 2015 (from 61.7% to 70.8%), while the proportion of those with self-reported brown skin color decreased. There was an increase in the proportion of primiparous mothers from 39.5% in 2004 to 44.4% in 2015. There was no difference in the period in the multiple pregnancy rate ($p = 0.187$). Among the complications of pregnancy, arterial hypertension and premature rupture of membranes were the most frequent in both cohorts. Prevalence of diabetes mellitus more than doubled, from 3.0% in 2004 to 7.5% in 2015 ($p < 0.001$). History of threatened miscrriage in the current pregnancy was reported by 10. 7% of the mothers in 2004 and 8.3% of the mothers in 2015 ($p < 0.001$). Cesarean section rate had an increase of more than 40% between 2004 and 2015.

None of the maternal characteristics were associated with the occurrence of multiple pregnancies in either of the two cohorts (Table 2). In 2004, the highest twinning rates occurred at the extremes of family income (1.5% of births in families earning ≤ 1.0 minimum wage and in families earning > 10 times the monthly minimum wage) and among mothers with less than four years of schooling (1.8%). In 2015, the highest rates were in families with higher monthly incomes (2.8% and 1.9%, respectively, in families that earned 6.1-10 and > 10 minimum wage) and among mothers ≥ 35 years of age (2.3%). The majority of twin births were by cesarean section

(78.6% in 2004 and 86.0% in 2015). In both cohorts, the majority of twin pregnancies failed to reach 37 weeks (61.9% in 2004 and 82.2% in 2015) (Table 3). In the 2004 cohort, the proportion of births at less than 34 weeks was more than six times higher in multiple pregnancies (19.0%) than in singleton pregnancies (3.0%); and births at 34 to 36 weeks were more than four times as frequent in newborns from multiple pregnancies (42.9%) than in singletons (10.6%). Meanwhile, in 2015, births at less than 34 weeks were 12 times more frequent in multiple pregnancies compared to singletons (41.1% *versus* 3.5%, respectively); and births from 34 to 36 weeks were four times more frequent among newborns from multiple pregnancies (41.1%) compared to singletons (10.3%). Comparing the two cohorts, the prevalence of births in multiple pregnancies prior to 34 weeks more than doubled from 2004 to 2015, from 19.0% to 41.1% (p = 0.03). The mean twin-to-twin interval in the nine pairs of twins born by vaginal delivery in 2004 was 8.56 minutes (SD= 9.15). In the 2015 cohort, the mean twin-to-twin interval in the seven pairs of twins born by vaginal delivery was 24.14 minutes (SD= 32.67) (p-value of the difference between cohorts = 0.002).

Table 4 compares second-born to first-born twins, and these to the newborns of singleton pregnancies from the same cohort, according to the mean birthweight and unfavorable perinatal outcomes. There was no difference between first- and second-born twins in the same cohort according to the target perinatal outcomes. In both cohorts, except for low 5-minute Apgar score, all the other indicators were more frequent in twins compared to singletons. Compared to the first- and second-born twins in 2004, the NICU admissions rates in 2015 were higher, respectively, in first-born (p=0.005) and second-born twins (p=0.04). In the 2004 cohort, there were 79 deaths in the first year of life, three of which were twins (Table 5), and in the 2015 cohort, among the 57 deaths in the first year of life, five were of twins. All twin deaths were of preterm twins. Neither cohort showed a difference between first- and second-born twins in IMR. Likewise, in the 2004 cohort there was no difference in IMR between twins and singletons. In the 2015 cohort, the IMR in first-born twins was similar to that of singletons, whereas among second-born twins, the PNMR was almost eight times (37.7:1,000 LB *versus* 4.8:1,000 LB) and the IMR six times higher than in singletons (75.4:1,000 LB *versus* 12.5:1000 LB).

Characteristics	**2004 Cohort (N=4,187)**	**2015 Cohort (N=4,220)**	**p***
Family income (MW)#	P < 0.001	P < 0.001	< 0.001
≤ 1.0	1,011 (24.1)	534 (12.7)	
1.1-3.0	1,833 (43.8)	1,991 (47.2)	
3.1-6.0	904 (21.6)	1,115 (26.4)	
6.1-10.0	244 (5.8)	316 (7.5)	
>10.0	195 (4.7)	262 (6.2)	
Schooling (years)	P < 0.001	P < 0.001	< 0.001
< 4	341 (8.2)	387 (9.1)	
8-Apr	2,016 (48.6)	1,084 (25.7)	

11-Sep	1,371 (33.1)	1,442 (34.2)	
≥ 12	417 (10.1)	1,306 (31.0)	
Age (years)	P < 0.001	P < 0.001	< 0.001
< 20	795 (19.0)	619 (14.7)	
20-24	1,136 (27.1)	998 (23.6)	
25-29	948 (22.7)	994 (23.6)	
30-34	748 (17.9)	988 (23.4)	
≥ 35	558 (13.3)	619 (14.7)	
Self-reported skin color	P <0.001	P <0.001	< 0.001
White	2,554 (61.7)	2,981 (70.8)	
Brown	903 (21.8)	570 (13.5)	
Black	682 (16.5)	661 (15.7)	
Parity	P <0.001	P <0.001	<0.001
Primipara	1,654 (39.5)	1,875 (44.4)	
Secondipara	1,097 (26.2)	1,270 (30.1)	
Multipara	1,435 (34.3)	1,073 (25.4)	
Type of pregnancy	P <0.001	P <0.001	0.187
Singleton	4,145 (99.0)	4,164 (98.7)	
Multiple	42 (1.0)	56 (1.3)	
Complications in the pregnancy			
Premature rupture of membranes	771 (18.4)	998 (23.6)	<0.001
Hypertensive disease	991 (23.7)	1,068 (25.3)	0.07
Gestational diabetes	124 (3.0)	317 (7.5)	<0.001
Threatened miscarriage	449 (10.7)	349 (8.3)	<0.001
Third-trimester bleeding	266 (6.4)	310 (7.4)	0.08
Type of delivery			<0.001
Vaginal	2,299 (54.9)	1,483 (35.2)	
Cesarean	1,888 (45.1)	2,736 (64.9)	

#MW – monthly minimum wage, approximately U$250 in 2015; *chi-square test for difference between the cohorts

Table 1: Maternal characteristics in the 2004 and 2015 Pelotas Birth Cohorts.

Characteristics	**2004 Cohort (N=4,187)**			**2015 Cohort (N=4,220)**		
	N	**Multiple Pregnancy**	**P***	**N**	**Multiple Pregnancy**	**P***
Family income (MW)#	4,187	42	0.338	4220	56	0.089
≤ 1.0	1,011	15 (1.5)		534	5 (0.9)	

1.1-3.0	1,833	15 (0.8)		1991	27 (1.4)	
3.1-6.0	904	8 (0.9)		1115	10 (0.9)	
6.1-10.0	244	1 (0.4)		316	9 (2.8)	
> 10.0	195	3 (1.5)		262	5 (1.9)	
Schooling (years)	4,145	41	0.316	4220	56	0.294
< 4	341	6 (1.8)		387	5 (1.3)	
8-Apr	2,016	22 (1.1)		1084	11 (1.0)	
11-Sep	1,371	10 (0.7)		1442	16 (1.1)	
≥ 12	417	3 (0.7)		1306	24 (1.8)	
Age (years)	4,185	42	0.5	4220	56	0.13
< 20	795	4 (0.5)		619	5 (0.7)	
20-24	1,136	12 (1.1)		998	10 (1.0)	
25-29	948	11 (1.2)		994	13 (1.3)	
30-34	748	10 (1.3)		988	15 (1.5)	
≥ 35	558	5 (0.9)		619	14 (2.3)	
Self-reported skin color	4,139	42	0.951	4220	56	0.642
White	2,554	27 (1.1)		2981	42 (1.4)	
Brown	903	8 (0.9)		570	8 (1.4)	
Black	682	7 (1.0)		661	5 (0.9)	
Parity	4,186	42	0.19	4220	56	0.694
Primipara	1,654	11 (0.7)		1875	23 (1.3)	
Secondipara	1,097	13 (1.2)		1270	16 (1.3)	
Multipara	1,435	18 (1.3)		1073	17 (1.6)	

[#]MW – monthly minimum wage, approximately U$250 in 2015; [*]chi-square test for difference within the cohort

Table 2: Multiple pregnancy rate in the 2004 and 2015 Pelotas Birth Cohorts.

		Gestational weeks		
		< 34 N (%)	**34-36 N (%)**	**≥ 37 N (%)**
2004 Cohort (N = 4,175)		P<0.001	P<0.001	P <0.001
	Multiple pregnancies (n=42)	8 (19.0)	18 (42.9)	16 (38.1)
	Singleton pregnancies (n=4,133)	124 (3.0)	436 (10.6)	3,573 (86.4)
2015 Cohort (N = 4,220)		P<0.001	P<0.001	P<0.001
	Multiple pregnancies (n=56)	23 (41.1)	23 (41.1)	10 (17.9)
	Singleton pregnancies (n=4,164)	147 (3.5)	428 (10.3)	3,588 (86.2)

Table 3: Gestational age at birth (weeks) in the 2004 and 2015 Pelotas Birth Cohorts.

	2004 cohort						**2015 cohort**					
Perinatal outcomes	**1st twin N=42**	**2nd twin N=42**	**Singleton N=4145**	**P1**	**P2**	**P3**	**1st twin N=53**	**2nd twin N=53**	**Singleton N=4,164**	**P1**	**P2**	**P3**
Mean birthweight, grams (SD)	2,358.0 (519.2)	2,226.5 (522.6)	3,167.5 (553.5)	0.251	<0.001	<0.001	2,098.5 (550.0)	2,066.0 (512.8)	3,197.9 (536.7)	0.755	<0.001	<0.001
Low birthweight, % (95%CI)4	57.1 (36.6-85.0)	69.1 (46.2-89.2)	9.1 (8.2-10.1)	0.366	<0.001	<0.001	75 (61.0-86.0)	78.8 (65.3-88.9)	8.3 (7.5-9.1)	0.816	<0.001	<0.001
Extremely low birthweight, % (95%CI)4	9.5 (2.6-24.4)	11.9 (3.9-27.8)	1.3 (1.0-1.7)	1	0.002	<0.001	17.3 (8.2-30.3)	13.5 (5.6-25.8)	0.9 (0.7-1.3)	0.787	<0.001	<0.001
5-minute Apgar < 7, % (95%CI)4	4.8 (0.6-17.2)	7.1 (1.5-20.9)	2.1 (1.7-2.6)	1	0.226	0.061	3.8 (0.5-13.0)	1.9 (0.1-10.1)	1.2 (0.9-1.6)	1	0.13	0.464
Admission to neonatal ICU, % (95%CI)4	14.3 (5.2-31.1)	23.8 (11.4-43.8)	5.8 (5.0-6.5)	0.405	0.033	<0.001	39.6 (26.4-54.0)	49 (35.1-63.2)	6.2 (5.5-7.0)	0.434	<0.001	<0.001

Table 4: Birthweight and frequency of unfavorable perinatal outcomes. Pelotas 2004 and 2015 Birth Cohorts.

	2004 cohort						**2015 cohort**					
	1st twin	**2nd twin**	**Singleton**	**P[1]**	**P[2]**	**P[3]**	**1st twin**	**2nd twin**	**Singleton**	**P[1]**	**P[2]**	**P[3]**
	N=42	**N=42**	**N=4,145**				**N=53**	**N=53**	**N=4,164**			
Neonatal mortality per 1,000 LB (95%CI)[4]	n = 1	n = 1	n = 48	1	0.477	0.477	n = 1	n = 2	n = 32	0.558	0.342	0.067
	23.8	23.8	11.6				18.9	37.7	7.7			
	(0.6-132.7)	(0.6-132.7)	(8.5-15.4)				(0.5-105.1)	(4.6-136.3)	(5.3-10.8)			
Post-neonatal mo-rtality per 1,000 LB (95%CI)[4]	n = 0	n = 1	n = 28	-	-	0.288	n = 0	n = 2	n = 20	-	-	0.038
	-	23.8	6.8				-	37.7	4.8			
		(0.6-132.7)	(4.5-9.8)					(4.6-136.3)	(2.9-7.4)			
Infant mortality	n = 1	n = 2	n= 76	0.625	0.721	0.229	n = 1	n = 4	n = 52	0.363	0.491	0.005
per 1,000 LB (95%CI)[4]	23.8	47.6	18.3				18.9	75.4	12.5			
	(0.6-132.7)	(5.8-172.0)	(14.4-22.9)				(0.5-105.1)	(20.6-193.2)	(9.3-16.4)			

[1]Difference between 1st and 2nd twins; [2]Difference between 1st twins and singletons; [3]Difference between 2nd twins and singletons; [4]95% CI: 95% confidence interval

Table 5: Neonatal, post-neonatal and infant mortality rates per 1000 Live Births (LB).

4. Discussion

This study showed that twins accounted for a small proportion of births in the 2004 and 2015 Pelotas Birth Cohorts (2.0% and 2.6%, respectively), but their contributions to the prematurity rate, NICU admissions, and infant mortality increased in this 11-year period. In 2004, twin pregnancies accounted for 4.4% of preterm births, whereas in 2015 they represented 7.5% of all preterm births, mainly at the expense of births < 34 weeks gestational age (increase of 122% from 2004 to 2015). The increase in prematurity among twins differs from the relative stability in the overall prematurity rate in births at Pelotas during this period (13.7% in 2004 and 13.8% in 2015) [19], and is consistent with pooled data showing a ninefold greater risk of preterm birth among multiples compared to singletons [21]. Previous studies showed that multiple pregnancies are the principal factor independently associated with spontaneous preterm births in Brazil [22], and twin pregnancies are also risk factors for medically induced preterm births [23].

Along with and consistent with the increase in preterm births, there was an increase in the proportion of twins who required NICU admission (independently of birth order) and who died in the first year of life, especially among second-born twins. The contribution of twins to infant mortality more than doubled in this period (from 4.0% in 2004 to 9.0% in 2015). Such a contribution was due not only to the decrease in the overall number of infant deaths in Pelotas during the period but also to the absolute increase in deaths among the twins. The increase in preterm deliveries during the study period probably had an important role in the mortality rate observed in twins from the 2015 cohort. Previous analyses of the Pelotas cohorts planned to assess the estimated change in neonatal and infant mortality after adjusting for the observed trends in gestational age distribution from 1982 to 2015 showed that the unadjusted infant mortality in 2015 was equal to 38% of that in 1982 (13.8:1000 LB and 36.4:1000 LB, respectively) [24]. After adjusting for distribution of gestational age the reduction was even greater: infant mortality in 2015 was 30% of that in 1980 [24].

There was no difference in twinning rates between the two cohorts, but the prevalence in 2015 (1.4%) was higher than in Rio Grande do Sul (the Brazilian state where Pelotas is located) (1.2%) ($p = 0.04$) and in Brazil as a whole from 2011 to 2014 (1.1%) ($p = 0.002$) [3]. This finding is consistent with the increase in maternal age and obesity in Pelotas in the last three decades, factors known to be associated with the occurrence of twin pregnancies as uncovered by other studies [25, 26]. The proportion of mothers 35 years or older in Pelotas increased from 9.9% in 1982 to 11.0%, 13.3%, and 14.7% in 1993, 2004, and 2015, respectively [27]. In 2015, multiple pregnancies were more frequent in mothers 35 years or older (2.3%). Additionally, during the same period, the prevalence of pregestational maternal obesity (BMI $\geq$ 30 kg/m^2) increased sharply, from 4.4% of mothers in 1982 to 4.9%, 9.0%, and 18.7% in 1993, 2004, and 2015, respectively [28].

Although black ethnicity, multiparity, and low socioeconomic status have been associated with multiple pregnancies in other studies [3], we found no difference in these factors in our two cohorts. On the contrary, in the 2015 cohort, mothers with the highest family incomes showed higher than average twinning rates. Results of previous analyses in the

2015 cohort showed that eighteen mothers gave birth to 23 newborns conceived by assisted reproduction procedures (in vitro fertilization in 70.6% of the cases), nine of them were newborns from multiple pregnancies [29]. In addition, a study that compared twinning rates in Pelotas from 1982 to 2015 showed a 220% increase among mothers with higher socioeconomic status and a 60% increase in white mothers, but no similar trend in brown or black mothers [30]. Also, singletons and twins formed through in vitro fertilization have independently higher risks of preterm birth than spontaneously conceived singleton and twin pregnancies [31].

As reported in other studies [5, 7-10], in the two cohorts the frequency of all unfavorable perinatal outcomes was higher in second-born than first-born twins. Although the difference in prevalence of LBW, extremely LBW and 5-minute Apgar <7 between first-born and second-born twins was statistically non-significant, all these rates were higher in second-born than in first-born twins. The lack of association is more likely due to lack of the study power than to an actual risk similarity between the two groups. The same was observed in terms of number of deaths. Although the difference in IMR between first-born and second-born twins was statistically non-significant, the number of deaths among the second-born twins in 2004 and 2015 were two- and four-fold higher, respectively, than that observed among the first-borns.

This study has strengths and limitations. The study's limitations include the lack of information on family history of multiple pregnancies, the small number of twin births and the relatively small number of deaths in both cohorts. Although the number of multiple births in our study corresponds to the totality of multiple births that occurred in Pelotas in 2004 and 2015, the absolute number of twin births was small and probably impaired the study power to detect statistical associations between maternal characteristics and type of pregnancy as well as between type of pregnancy and the outcomes. The small sample size also prevented comparing perinatal outcomes and mortality between first- and second-born twins according to gestational age and type of delivery, which are important prognostic characteristics for twins' survival, as previously reported [7]. Meanwhile, the strengths of the present study include the population-based nature of the two birth cohorts, the low rate of attrition and the consistency of methods employed over the period. Data collected for each twin separately at the time of birth is also a strength mainly considering that information on second-born twins tends to be insufficient, especially when obtained from hospital medical records [32]. In addition, the mothers and twins were analyzed separately, and the first- and second-born twins were analyzed individually according to frequency of unfavorable perinatal outcomes and mortality in the first year of life.

5. Conclusion

This study showed that the prevalence of twin births remained stable in the eleven-year period, whereas the prevalence of births in multiple pregnancies prior to 34 weeks more than doubled from 2004 to 2015. Furthermore, in the 2015 cohort, the post-neonatal and the infant mortality rates in second-born twins were, respectively, eight and six times higher than in singletons. Although the prevalence and consequences of twin pregnancies may vary from place to place, the results of this study could serve as a reference for the planning of health resources and development of preventive strategies targeting twin infants born in Pelotas and in settings with similar sociodemographic and health services structure characteristics.

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Conflicts of Interest

The authors have no conflicts to declare.

Authors’ Contributions

ISS, NCJV and GS were responsible for the study’s conception. NCJV and GS performed the statistical analyses. ISS contributed to interpretation of the results and wrote the first version of the article. MFS, AM, ADB, MD, IMK, and FCB critically analyzed the article and made important intellectual contributions to the content. All authors read and approved the final manuscript.

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